capillary injury. This process is biological, with reversible and irreversible pathways[4,5] and along a spectrum that cannot be dichotomous, hence the association of time, arterial oxygen tension/inspired oxygen fraction (Pao_2/Fio_2) ratios and radiographic findings that are in the context of the International Society of Heart and Lung Transplantation definition. The authors do not reveal their perioperative bronchoscopy protocol, which itself can influence radiographic findings with respect to presence or absence of infiltrates. It is not uncommon that infiltrates could be due to segmental and/or subsegmental mucus plugging, which when it extends to main bronchi can cause significant ventilation–perfusion mismatch and reduction of Pao_2/Fio_2 ratios. The population sample, as quite correctly stated by the authors, remains small and heterogeneous; primary pulmonary hypertension is a bilateral problem and requires bilateral lung transplantation. The authors should analyze their findings with respect to a clean cohort of infectious lung disease, for example, to avoid the confounding effect of pulmonary hypertension. The reader will soon realize that the majority of patients with pulmonary hypertension were among the cohort with bilateral infiltrates.

Moreover, patients with fixed pulmonary hypertension are more likely to experience reperfusion–ischemic injury with higher PGD grades.[5] Recently, aprotinin has been shown to reduce reperfusion injury and allograft dysfunction. It is unclear from the manuscript which antifibrinolytic was administered during transplantation—the type of antifibrinolytic being a potential confounder. The authors state that unilateral infiltrates were associated with PGD grade 3, but that diminished at T48 hours. However, when compared with the absence of infiltrates at T0, it had decreased. It may be more appropriate to look at the absolute difference from T0 to T48 rather than the relative difference, which in a larger homogeneous population sample would minimize confounding. Short of radiographic findings, a clinician can be at loss if Pao_2/Fio_2 ratios are the only information provided to make a diagnosis of PGD and/or to intervene with medical therapy or bronchoscopy. Given the therapeutic and diagnostic power of bronchoscopy, any infiltrate on the chest radiograph is of paramount importance in decision making and detection of this biological PGD process. Furthermore, despite the inherently subjective interpretation of a chest radiograph, a transplant physician can recognize patterns of unilateral infiltrates that are typical of the most severe and rapidly progressing to grade 3 PGD, which could go unnoticed if only bilateral infiltrates are considered.

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Reply to the Editor:

The aims of our study were to describe the difference of unilateral and bilateral radiographic infiltrates on early posttransplant outcomes, including primary graft dysfunction (PGD) grade.[1,2] As Shuhaiber states, a perioperative bronchoscopy protocol could influence radiographic findings. In our protocol, inspection and toileting bronchoscopy was routinely performed before donor lung procurement, immediately after implantation, and within 6 hours after admission to the intensive care unit. Therefore, significant airway secretions or mucus plugging were unlikely to be present in the early postoperative period. Moreover, for the purpose of PGD grading, only radiographic infiltrates, consistent with pulmonary edema rather than atelectasis, were assessed (as per the International Society for Heart and Lung Transplantation PGD grading guideline.[2]).

Notwithstanding, mucus plugging, clot, or extubation itself[3] could cause a temporary reduction of arterial oxygen tension/fraction of inspired oxygen (Pao_2/Fio_2) ratio. Therefore, the worst Pao_2/Fio_2 ratio might not represent true graft function[4] and should not be used for PGD grading.

Pulmonary hypertension (PH) is a significant risk factor for posttransplant radiographic infiltrates. In our study, the number of patients with PH was small; thus, the majority of bilateral infiltrates were seen in the non-PH patient group. Moreover, the official PGD grading system applies to both PH and non-PH recipients.

Antifibrinolytic agents were used for patients having a higher risk of bleeding (eg, cardiopulmonary bypass, previous thoracic operation), patients already at increased risk of postoperative pulmonary infiltrates. Therefore, in this circumstance, the radiographic infiltrates are potentially multifactorial.

Although further study including multivariate analysis is needed, our study clearly showed that the early posttransplant outcome of the unilateral infiltrates was similar to that in the group having a clear chest x-ray film and significantly better than that in those with bilateral infiltrates. Therefore, we believe that in bilateral lung transplantation, only bilateral infiltrates should be used as part of the definition of PGD.

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Amiodarone and cardiac surgery

To the Editor:

The recent publication of a large randomized trial of amiodarone arrhythmia prophylaxis after cardiac surgery (PAPABEAR) is of great interest.[1] It was striking how similar the results of this trial were to our previous observational analysis of perioperative amiodarone during mitral valve repair,[2] and a detailed comparison raises several points. First, both studies concluded that amiodarone was effective, reducing postoperative atrial arrhythmias by half and virtually eliminating mortality from ventricular arrhythmias. Second, serious complications of a brief perioperative administration were rare. In PAPABEAR, bradycardia requiring dose reduction occurred in 5.7% of cases and was considered a side effect. In clinical practice, however, postoperative bradycardia can be managed easily with transient atrial pacing, and reduction to a low discharge dose is routine. Third, only low-risk patients undergoing elective procedures were randomly assigned in PAPABEAR, which limited event rates and statistical power to define other clinical benefits, similar to the AFIST trial.[3] The use of large national databases for such studies could allow better sample sizes and would certainly be less costly. The patients most likely to achieve absolute event reductions are those at the very highest risk (ie, those most prone to nonfatal and fatal arrhythmias). Those patients often undergo operation on an emergency basis and thus are not candidates for a prolonged preoperative oral protocol.

In the acute setting, 12 hours of standard intravenous loading (150-mg intravenous bolus followed by 1-mg/min intravenous infusion for 6 hours and then 0.5-mg/min intravenous infusion) performs well,[2] similar to the "hybrid" protocol of AFIST II.[4] The infusion is continued postoperatively, and additional 150-mg bolus doses are administered aggressively for persistent sinus tachycardia or the appearance of arrhythmias. Dose reductions are prompted by (1) observed lengthening of the P-R or Q-T interval or (2) reduction in the underlying sinus rate to 70 to 80 beats/min. Oral amiodarone is begun on the first postoperative day at 400 mg orally every 6 hours, and the intravenous agent is overlapped for 24 hours. Then, the oral dose is progressively reduced to 200 mg orally twice daily at discharge, again guided by optimizing the sinus rate to 70 to 80 beats/min. If the sinus rate is especially sensitive to the drug, the discharge dose can be reduced all the way to 100 mg orally daily. The discharge dose is continued orally for 3 to 4 weeks after surgery to prevent the occasional "late breakthrough" and then stopped abruptly, because amiodarone has a prolonged effect after discontinuation. If sinus tachycardia is difficult to control, very low doses of β-blockers can be added with synergistic effect.

After using this approach for more than 10 years,[2] it is now routine for all cardiac procedures, with a clinical experience that parallels PAPABEAR. Absolute benefits, however, are even more impressive in high-risk patients. Aggressive and routine arrhythmia prophylaxis with this safer and more effective agent has been a major advance in the care of cardiac surgical patients. This approach could significantly reduce the current rate of postoperative arrhythmias, which have occurred in as many as a third of cardiac patients in recent series.[5]

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